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51. (New) A peptide nucleic acid conjugate of claim 37 wherein one of Q or I comprises a conjugate, wherein said conjugate is polylysine.

52. (New) A peptide nucleic acid conjugate of claim 37 wherein one of A, A_m, L or L_m comprises a conjugate, wherein said conjugate is polylysine.

Remarks

Claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37 and 39-50 are pending in this application. Claims 24, 30, 33 and 37-50 have been amended. No new matter has been added. New claims 51 and 52 find support in the specification at, for example, page 17, lines 33-36.

Applicants thank the Examiner for the courtesy afforded Applicants' undersigned attorney in an interview held on February 21, 2001, in which several issues regarding the rejections of record were clarified.

Claims 8-10, 12, 13, 15, 20, 22-24, 30-33, 37 and 39-50 are rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. These claims have been amended in accordance with the suggestion in the Office Action. Thus, the rejection is believed to be overcome.

Claims 24 and 33 are rejected under 35 U.S.C. § 112, fourth paragraph, for failing to further limit the subject matter of the previous claim. In view of Applicants' amendment of these claims to recite that a is 1, the rejection is believed to be overcome.

Claims 1, 5, 8-10, 12, 13, 15, 230, 22-24, 30-33, 37, 39-43, 45, 46, 48 and 50 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,705,333 to Shah et al.

("Shah et al."). The Office Action asserts that the presently claimed structures are a species of the Shah et al. PENAM conjugates structures. Applicants respectfully request withdrawal of the rejection, as the priority document contains the subject matter purported to be disclosed by Shah et al. Thus, Shaw et al. is not properly applied as prior art against the present claims.

The present application claims priority benefit of, *inter alia*, U.S. application Ser. No. 08/108,591, filed November 22, 1993 (hereinafter "the 591 priority application").^{1,2} Applicants note that the Office Action has carefully compared the Shah et al. backbone structures to those of the present claims. However, as the presently claimed backbone structure finds support in the 591 priority application, the disclosure of a similar structure in Shah et al. is irrelevant.

In addition, the 591 priority application also discloses various conjugate groups that can be appended to the PNA, including those that the Office Action asserts are disclosed in the Shah et al. reference. Specifically, the Office Action points to Shah et al. at column 19, lines 17-50 as disclosing conjugate groups that are equivalent to the presently claimed crosslinking agents, alkylating agents, cleaving groups, and metal chelators. However, the 591 priority application discloses each of these classes of conjugate groups. For example, the 591

¹ This application, like the present application, is in prosecution before Examiner Marschel and is therefore presumed to be available to the Examiner.

² Applicants have discovered that the Declaration and specification in the present application incorrectly refer to the filing date of the 591 priority application as being August 27, 1993, instead of the correct date stated above. Applicants will submit a new declaration with the correct date in due course.

priority application discloses PNA conjugated to lysine (which has been previously been characterized by the Examiner as a crosslinking agent) in, for example, Example 8 and in various other examples in the specification. The 591 priority applicaiton additionally discloses conjugate groups having alkylator activity and conjugate groups having nuclease (e.g., cleaving) activity at page 17, lines 13-15. The 591 priority application additionally discloses chelator conjugate groups at page 9, lines 22-25. Thus, the 591 priority application discloses the pertinent disclosure of the Shah et al. reference. Accordingly, the Shah et al. reference is not prior art against the present claims under 35 U.S.C. § 103(a). See *In re Stryker*, 168 U.S.P.Q. 372 (C.C.P.A. 1971).

The Office Action also, as best understood, appears to assert on page 5 that the constituent nucleobases of the PENAM (or, presumably, of the claimed PNAs) qualify as reporters by virtue of their detectability by UV light, or as aromatic lipophilic moieties. However, with respect, Applicants assert that those skilled in the art, reading the specification, would readily understand that the constituent nucleobases of the claimed PNA structures, which serve to participate in, for example, Watson-Crick or Hoogsteen type binding, are distinct from the appended conjugate groups of the PNA. Moreover, the 591 priority application discloses reporter groups at page 17, line 16, and also discloses nucleobases at numerous places throughout the specification. Thus, even if one were to attempt to argue that the Shah et al. PENAM nucleobases are conjugate groups according to the claims, (a position with which, as pointed out above, Applicants would disagree), such disclosure is not prior art against the present claims because the 591 priority application discloses such nucleobases.

In view of the preceding discussion, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 8-10, 15, 20, 22-24, 30-33, 37, 40, 41 and 45-50 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,623,049 to Lobberding et al. ("Lobberding et al."). The Office Action asserts that Lobberding et al. discloses PNA structures of the claims and crosslinking agents. However, as discussed above, the 591 priority application discloses these features. Inasmuch as the Lobberding et al. reference was filed on September 6, 1994, well after the date of the 591 priority application, the Lobberding et al. disclosure is not prior art against the present claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

The Office Action rejects various claims for alleged obvious-type double patenting over several issued patents, and provisionally rejects various claims over several pending applications. Specifically, claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, 39-43 and 45-50 are rejected over claims 1-3 of U.S. Patent No. 5,539,082; claims 1, 5, 8-10, 12, 13, 15, 20, 37, 39-41 and 47-47 are rejected over claim 1 of U.S. Patent No. 5,773,571; claim 50 is rejected over claims 1, 5, and 8 of U.S. Patent No. 5,786,461; claims 8-10, 15, 20, 30-33, 37, 40, 41 and 47-49 are rejected over claims 1 and 9 of U.S. Patent No. 5,719,262; claims 8-10, 15, 20, 30-33, 37, 40, 41, and 47-49 are provisionally rejected over claims 4, 5, 9 and 40 of copending U.S. application ser. no. 08/108,591; claims 1, 5, 8-10, 12, 13, 15, 20, 37, 39-41 and 47-49 are provisionally rejected over claims 2, 6, 7, 9, 22, 24, 25, 27, 35, 37-39 and 44 of copending U.S. application ser. no. 08/275,951 taken in view of Switzer et

al., Bioch. 32:10489 (1993); claims 22-24, 45, 46 and 50 are provisionally rejected over claims 8, 34, 35, 37, 40-47, 49-51, 53-56, 61-63, 66-69, 71-76 and 89-93 of copending U.S. application ser. no. 08/468,719; claims 1, 5, 8-10, 15, 20, 30-33, 37, 40, 41 and 47-49 are provisionally rejected over claims 1, 5 and 13 of copending U.S. application ser. no. 08/686,114 taken in view of WO 86/05518 Summerton et al.; claims 1, 5, 8-10, 12, 13, 15, 20, 37, 39-41 and 47-49 are provisionally rejected over claims 2, 6, 7, 34, 35, 38, 40 and 42 of copending U.S. application ser. no. 08/765,798 taken in view of Switzer et al., Bioch. 32:10489 (1993); and claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37 and 39-50 are provisionally rejected over claims 24, 26 and 28 of copending U.S. application ser. no. 09/106,667. Applicants will address each of these rejections upon an indication of otherwise allowable subject matter in the present application.

Applicants believe that the claims presently before the Examiner patentably define the invention over the art of record and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment.

The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,



Michael P. Straher
Reg. No. 38,325

Date: May 25, 2001

WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
(215) 568-3100

VERSION WITH MARKINGS TO SHOW CHANGES MADE

The pedigree of the application on page 1 has been amended in line 4 as follows:

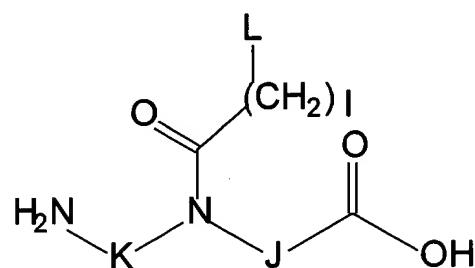
This application is a continuation-in-part of United States application serial number 08/108,591, filed [Aug. 27] November 22, 1993 that, in turn, is a national phase application of PCT application EP/01219, filed May 22, 1992, claiming priority to Danish Patent Applications: No. 986/91, filed May 24, 1991, No. 987/91, filed May 24, 1991, and No. 510/92, filed April 15, 1992. In addition, this application is a continuation-in-part to United States application serial number 08/088,658, filed July 2, 1993, United States application serial number 08/088,661, filed July 2, 1993 and United States application serial number 08/275,951, filed July 15, 1994.

In the claims:

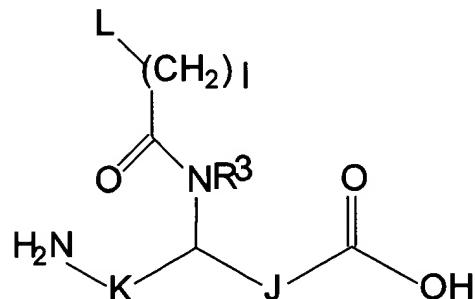
Claims 24, 30, 33 and 37-50 have been amended as follows:

24. (Amended) A peptide nucleic acid conjugate of claim 21 wherein [R^{13} is a conjugate] a is 1.

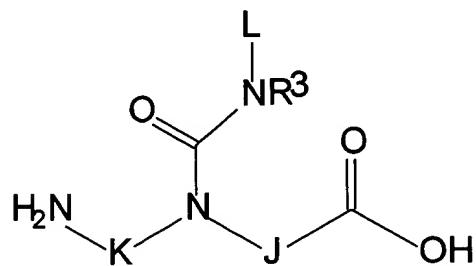
30. (Thrice amended) A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:



or formula:



or formula:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13} , if present, is a conjugate; and

a is 0 or 1;

K is $(CR^6R^7)_z$;

J is $(CR^6R^7)_y$; wherein:

R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino;

R^5 is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C_1-C_6) alkyl; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

l is an integer from 1 to 5; and

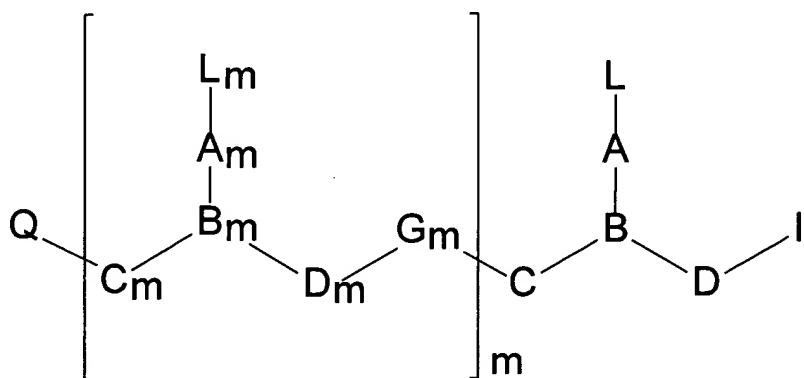
at least one of L and R3 comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a

metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety.

33. (Amended) A peptide nucleic acid conjugate of claim 30 wherein [R¹³ is a conjugate] a is 1.

37. (Twice Amended) A peptide nucleic acid conjugate of the formula:



wherein:

m is an integer from 1 to about 50;

L and L_m independently are R¹²(R¹³)_a wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13} , if present, is a conjugate; and
a is 0 or 1;

C and C_m independently are $(CR^6R^7)_y$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 , SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

wherein R^5 is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6) alkyl; and

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino;

D and D_m independently are $(CR^6R^7)_z$;

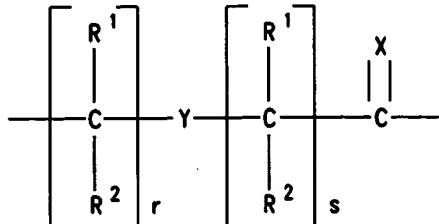
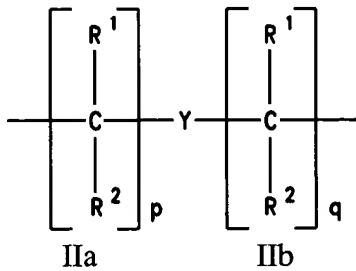
each of y and z is zero or an integer from 1 to 10,
wherein the sum y + z is greater than 2 but not more than 10;

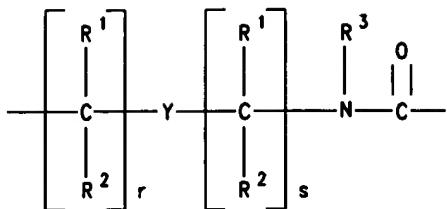
G_m is independently $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$, or
 $-NR^3SO_2-$ in either orientation;

each pair of $A-A_m$ and $B-B_m$ are selected such that:

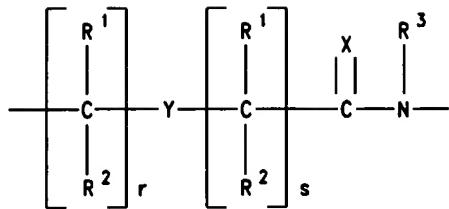
(a) A or A_m is a group of formula (IIa), (IIb) or
(IIc) and B or B_m is N or R^3N^+ ; or

(b) A or A_m is a group of formula (IId) and B or B_m is
CH;





IIc



IIId

wherein:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

R¹ and R² independently are hydrogen, (C₁-C₄)alkyl, hydroxy-substituted (C₁-C₄)alkyl, alkoxy-substituted (C₁-C₄)alkyl, alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

I is -NR⁸R⁹ or -NR¹⁰C(O)R¹¹; wherein:

R⁸, R⁹, R¹⁰ and R¹¹ independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

Q is -CO₂H, -CO₂R⁸, -CO₂R⁹, -CONR⁸R⁹, -SO₃H, -SO₂NR¹⁰R¹¹ or an activated derivative of -CO₂H or -SO₃H; and

wherein:

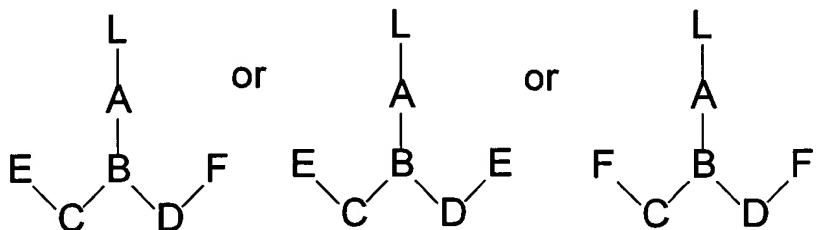
at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m, L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein when said Q or I is a crosslinking agent, said crosslinking agent is not lysine.

38. (Twice Amended) A compound having one of the following formulas:



wherein:

L is R¹²(R¹³)_a; wherein:

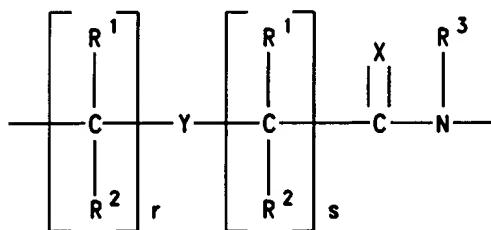
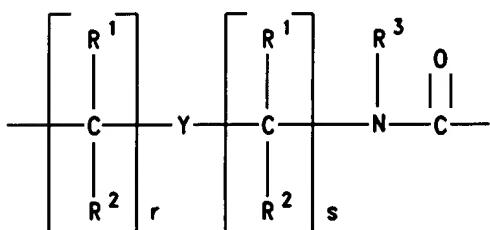
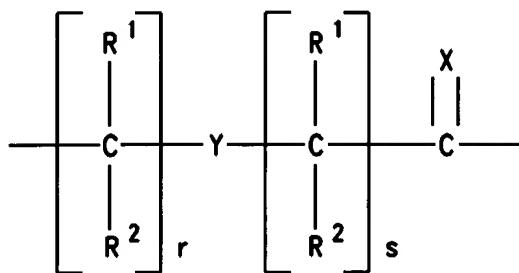
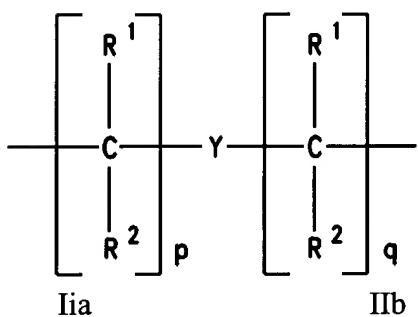
R¹² is hydrogen, hydroxy, (C₁-C₄) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13} , if present, is a conjugate; and
a is 0 or 1;

A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+ ; or

(b) A is a group of formula (IId) and B is CH;



IIc IId

where:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, (C₁-C₄)alkyl, hydroxy-substituted (C₁-C₄)alkyl, alkoxy-substituted (C₁-C₄)alkyl, alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_y$;

D is $(CR^6R^7)_z$; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴ and SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio or amino; and

R⁵ is hydrogen, a conjugate, (C₁-C₆) alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆) alkyl; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

F independently is NHR³ or NPgR³, where Pg is an amino protecting group;

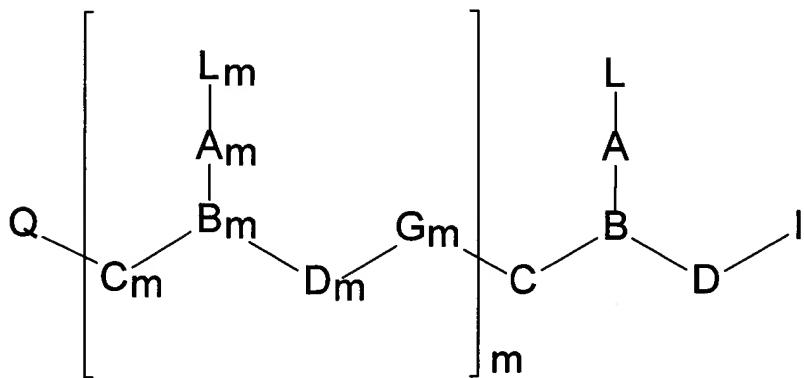
or

F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety.

39. (Amended) A peptide nucleic acid conjugate of the formula:



wherein:

m is an integer from 1 to about 50;

L and L_m independently are R¹²(R¹³)_a wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R¹³, if present, is a conjugate; and

a is 0 or 1;

C and C_m independently are (CR⁶R⁷)_y; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid,

(C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy,

(C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴, SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

wherein R⁵ is hydrogen, a conjugate, (C₁-C₆)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C₁-C₆)alkyl; and

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio or amino;

D and D_m independently are (CR⁶R⁷)_z;

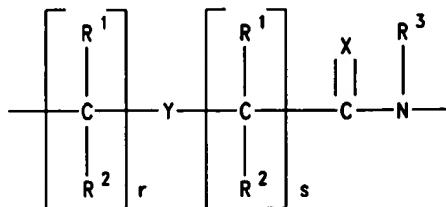
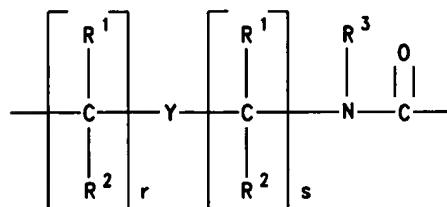
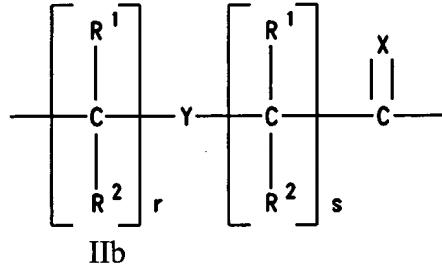
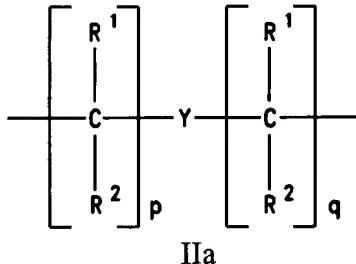
each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10;

G_m is independently -NR³CO-, -NR³CS-, -NR³SO-, or -NR³SO₂- in either orientation;

each pair of A-A_m and B-B_m are selected such that:

(a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R³N⁺; or

(b) A or A_m is a group of formula (IId) and B or B_m is CH;



wherein:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

R¹ and R² independently are hydrogen, (C₁-C₄) alkyl, hydroxy-substituted (C₁-C₄) alkyl, alkoxy-substituted (C₁-C₄) alkyl, alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

I is -NR⁸R⁹ or -NR¹⁰C(O)R¹¹; wherein:

R⁸, R⁹, R¹⁰ and R¹¹ independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

Q is -CO₂H, -CO₂R⁸, -CO₂R⁹, -CONR⁸R⁹, -SO₃H, -SO₂NR¹⁰R¹¹ or an activated derivative of -CO₂H or -SO₃H; and

wherein:

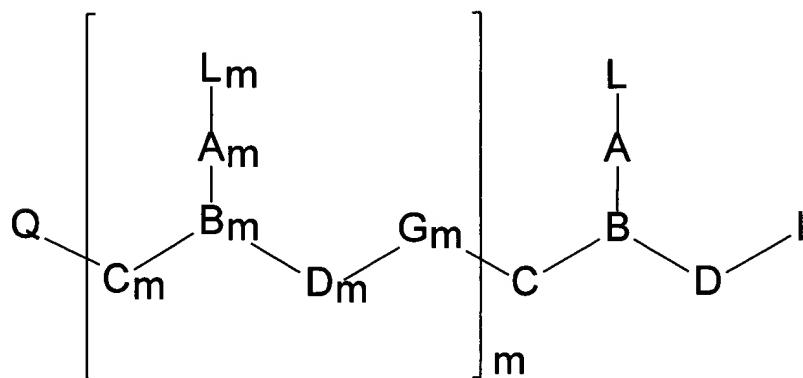
at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m, L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R¹, R² or R³ is a conjugate.

40. (Amended) A peptide nucleic acid conjugate of the formula:



wherein:

m is an integer from 1 to about 50;

L and L_m independently are R¹²(R¹³)_a wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R¹³, if present, is a conjugate; and

a is 0 or 1;

C and C_m independently are (CR⁶R⁷)_y; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid,

(C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴, SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

wherein R⁵ is hydrogen, a conjugate, (C₁-C₆) alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C₁-C₆) alkyl; and

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio or amino;

D and D_m independently are (CR⁶R⁷)_z;

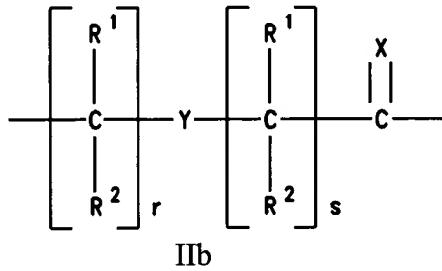
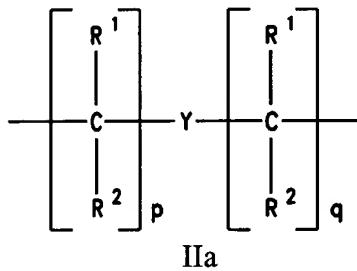
each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10;

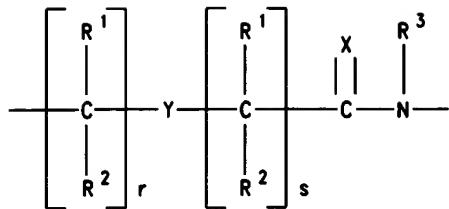
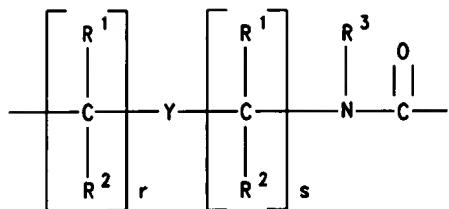
G_m is independently -NR³CO-, -NR³CS-, -NR³SO-, or -NR³SO₂- in either orientation;

each pair of A-A_m and B-B_m are selected such that:

(a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R³N⁺; or

(b) A or A_m is a group of formula (IID) and B or B_m is CH;





wherein:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

R¹ and R² independently are hydrogen, (C₁-C₄)alkyl, hydroxy-substituted (C₁-C₄)alkyl, alkoxy-substituted (C₁-C₄)alkyl, alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

I is -NR⁸R⁹ or -NR¹⁰C(O)R¹¹; wherein:

R⁸, R⁹, R¹⁰ and R¹¹ independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

Q is -CO₂H, -CO₂R⁸, -CO₂R⁹, -CONR⁸R⁹, -SO₃H, -SO₂NR¹⁰R¹¹ or an activated derivative of -CO₂H or -SO₃H; and

wherein:

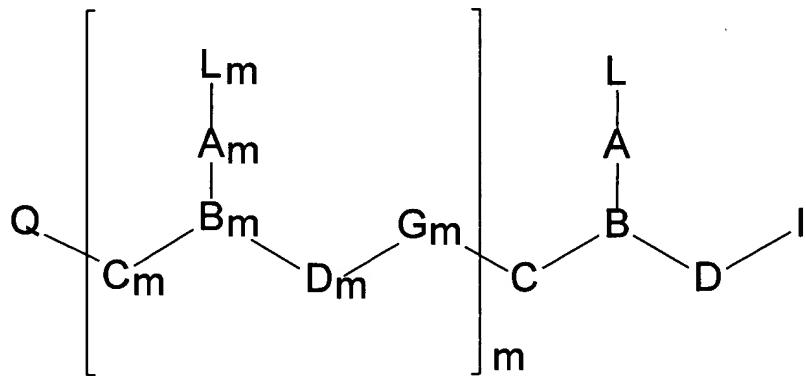
at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m, L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R⁸, R⁹, R¹⁰ and R¹¹ is a conjugate.

41. (Amended) A peptide nucleic acid conjugate of the formula:



wherein:

m is an integer from 1 to about 50;

L and L_m independently are R¹²(R¹³)_a wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R¹³, if present, is a conjugate; and
a is 0 or 1;

C and C_m independently are (CR⁶R⁷)_y; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴, SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

wherein R⁵ is hydrogen, a conjugate, (C₁-C₆) alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C₁-C₆) alkyl; and

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio or amino;

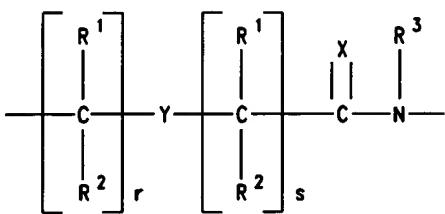
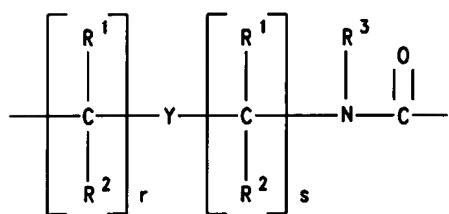
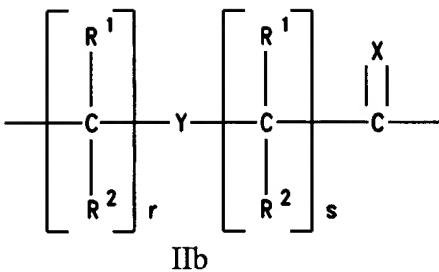
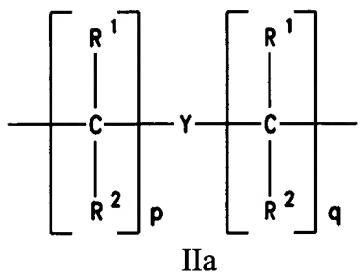
D and D_m independently are (CR⁶R⁷)_z;

each of y and z is zero or an integer from 1 to 10,
wherein the sum y + z is greater than 2 but not more than 10;

G_m is independently -NR³CO-, -NR³CS-, -NR³SO-, or -NR³SO₂- in either orientation;

each pair of A-A_m and B-B_m are selected such that:

- (a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R³N⁺; or
- (b) A or A_m is a group of formula (IID) and B or B_m is CH;



wherein:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

R¹ and R² independently are hydrogen, (C₁-C₄)alkyl, hydroxy-substituted (C₁-C₄)alkyl, alkoxy-substituted (C₁-C₄)alkyl, alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

I is -NR⁸R⁹ or -NR¹⁰C(O)R¹¹; wherein:

R⁸, R⁹, R¹⁰ and R¹¹ independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

Q is -CO₂H, -CO₂R⁸, -CO₂R⁹, -CONR⁸R⁹, -SO₃H, -SO₂NR¹⁰R¹¹ or an

activated derivative of -CO₂H or -SO₃H; and

wherein:

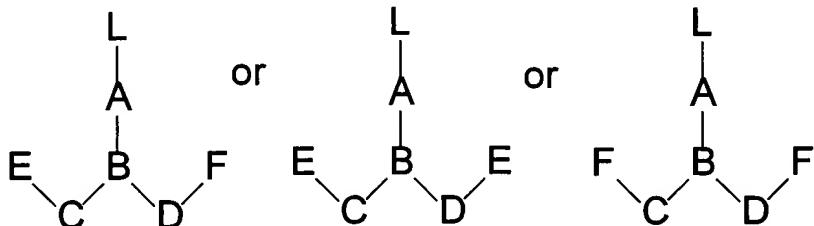
at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m, L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R³, R⁴, R⁵, R⁶ and R⁷ is a conjugate.

42. (Amended) A peptide nucleic acid conjugate of formula:



wherein:

L is R¹²(R¹³)_a; wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a

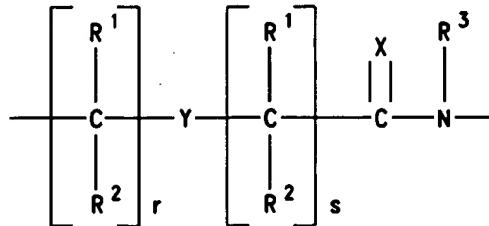
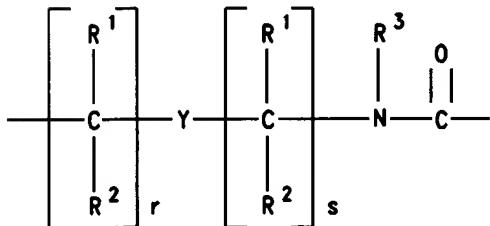
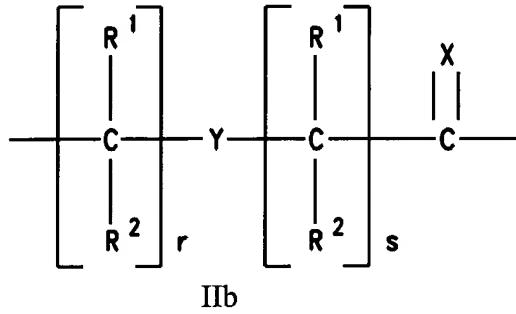
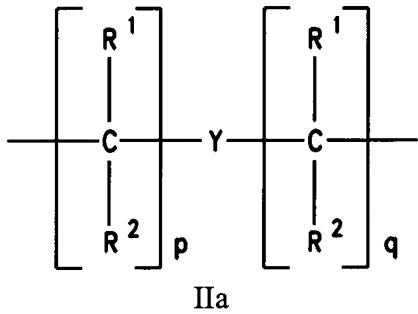
heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R¹³, if present, is a conjugate; and
a is 0 or 1;

A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R³N⁺; or

(b) A is a group of formula (IId) and B is CH;



where:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R¹ and R² independently are hydrogen, (C₁-C₄) alkyl, hydroxy-substituted (C₁-C₄) alkyl, alkoxy-substituted (C₁-C₄) alkyl, alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is (CR⁶R⁷)_y;

D is (CR⁶R⁷)_z; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴ and SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio or amino; and

R⁵ is hydrogen, a conjugate, (C₁-C₆) alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆) alkyl; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

F independently is NHR³ or NPgR³, where Pg is an amino protecting group; or

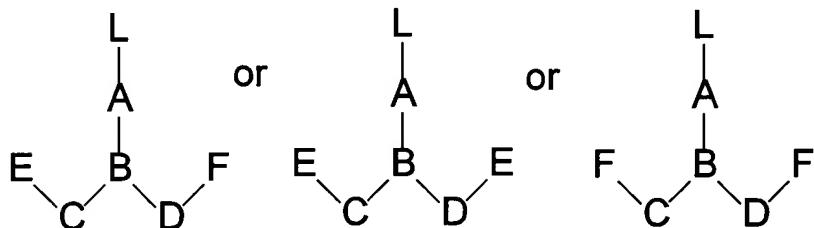
F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble

vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and
 wherein said conjugate optionally includes a linking moiety; and

wherein at least one group R³ is a conjugate.

43. (Amended) A peptide nucleic acid conjugate of formula:



wherein:

L is R¹²(R¹³)_a; wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

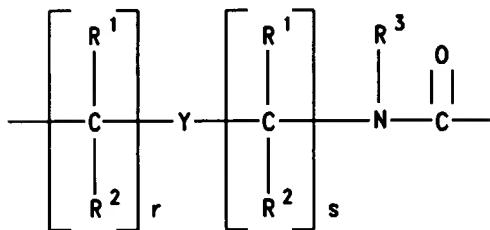
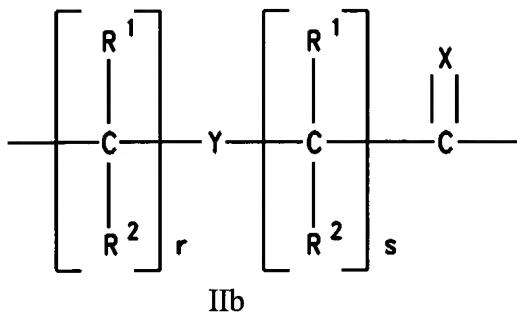
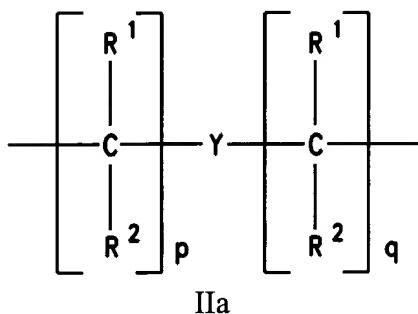
R¹³, if present, is a conjugate; and

a is 0 or 1;

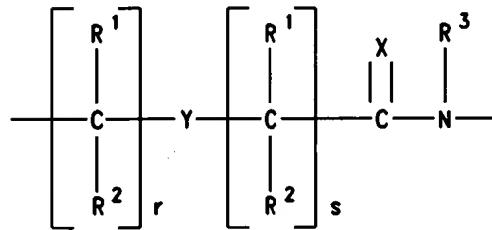
A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and
 B is N or R³N⁺; or

(b) A is a group of formula (IIId) and B is CH;



IIc



IIId

where:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R¹ and R² independently are hydrogen, (C₁-C₄) alkyl, hydroxy-substituted (C₁-C₄) alkyl, alkoxy-substituted (C₁-C₄) alkyl, alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is (CR⁶R⁷)_y;

D is (CR⁶R⁷)_z; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴ and

SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system; R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio or amino; and R⁵ is hydrogen, a conjugate, (C₁-C₆)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆)alkyl; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

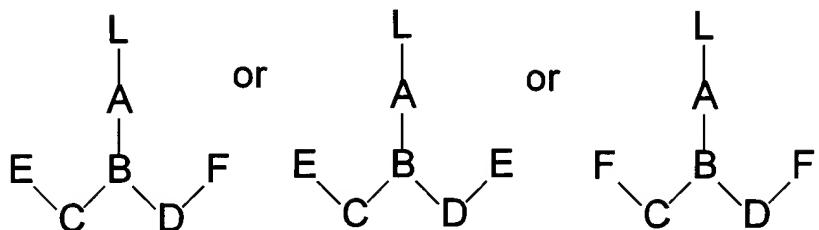
E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

F independently is NHR³ or NPgR³, where Pg is an amino protecting group; or

F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a linking moiety; and wherein at least one of said groups A or said groups B include a conjugate.

44. (Amended) A peptide nucleic acid conjugate of formula:



wherein:

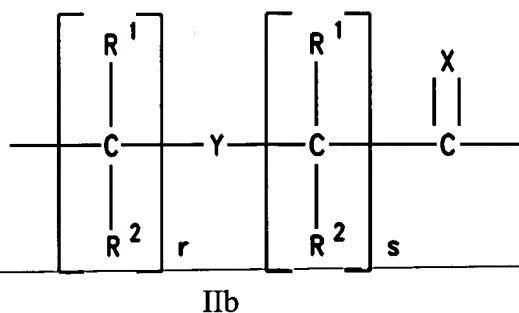
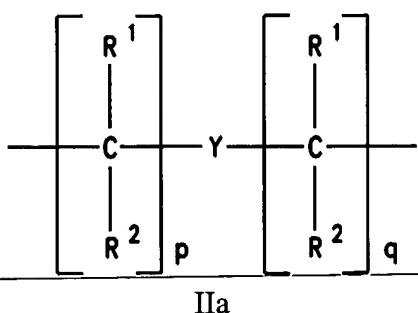
L is $R^{12}(R^{13})_a$; wherein:

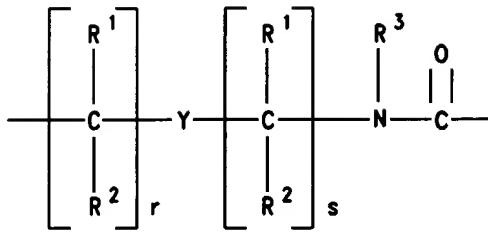
R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13} , if present, is a conjugate; and
a is 0 or 1;

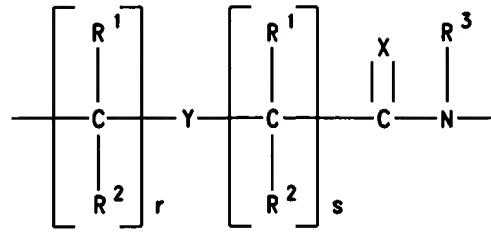
A and B are selected such that:

- (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+ ; or
- (b) A is a group of formula (IId) and B is CH;





IIc



IIId

where:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R¹ and R² independently are hydrogen, (C₁-C₄)alkyl, hydroxy-substituted (C₁-C₄)alkyl, alkoxy-substituted (C₁-C₄)alkyl, alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is (CR⁶R⁷)_y;

D is (CR⁶R⁷)_z; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆)alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆)alcoxy, (C₁-C₆)alkylthio, a conjugate, NR³R⁴ and SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio or amino; and

R⁵ is hydrogen, a conjugate, (C₁-C₆)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

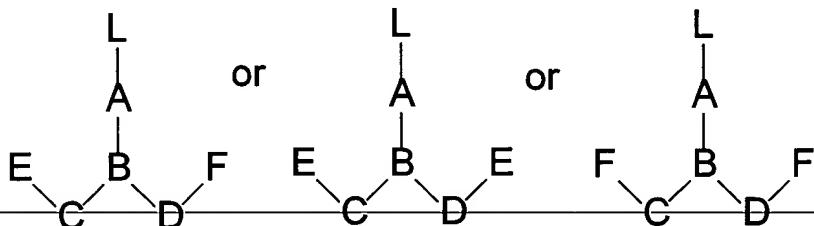
F independently is NHR³ or NPgR³, where Pg is an amino protecting group; or

F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a linking moiety; and

wherein at least one of group R¹ or group R² is a conjugate.

45. (Amended) A peptide nucleic acid conjugate of formula:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

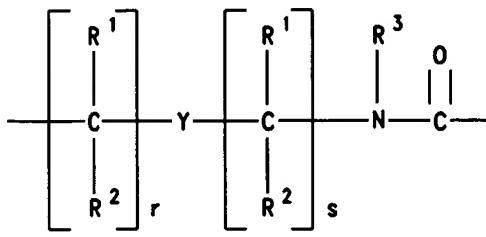
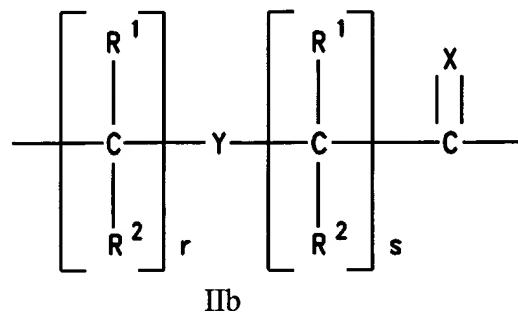
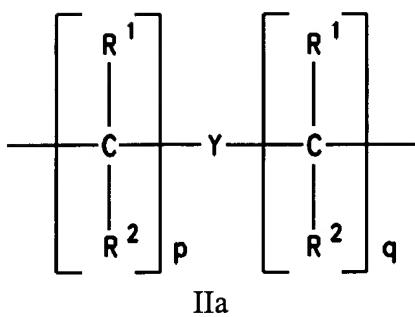
R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13} , if present, is a conjugate; and
 a is 0 or 1;

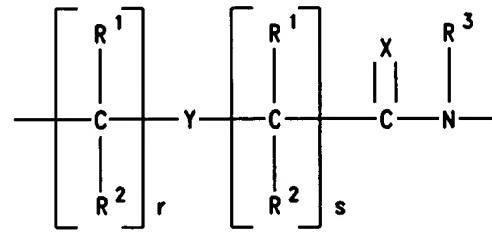
A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+ ; or

(b) A is a group of formula (IId) and B is CH;



IIc



IId

where:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;
Y is a single bond, O, S or NR⁴;
p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R¹ and R² independently are hydrogen, (C₁-C₄) alkyl, hydroxy-substituted (C₁-C₄) alkyl, alkoxy-substituted (C₁-C₄) alkyl, alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is (CR⁶R⁷)_y;

D is (CR⁶R⁷)_z; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴ and SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio or amino; and

R⁵ is hydrogen, a conjugate, (C₁-C₆) alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆) alkyl; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

F independently is NHR³ or NPgR³, where Pg is an amino protecting group; or

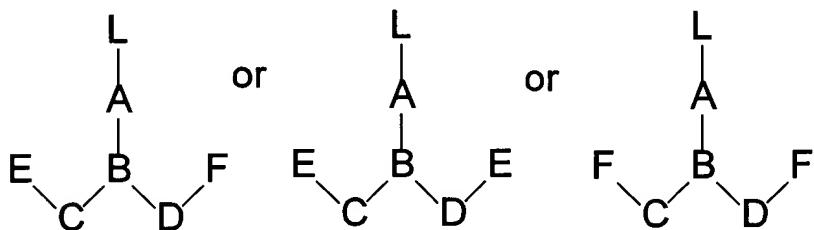
F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a

water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R³, R⁴, R⁵, R⁶, and R⁷ is a conjugate.

46. (Amended) A peptide nucleic acid conjugate of formula:



wherein:

L is R¹²(R¹³)_a; wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R¹² is a naturally

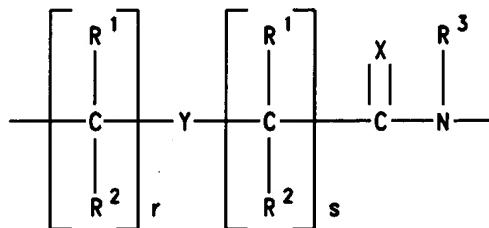
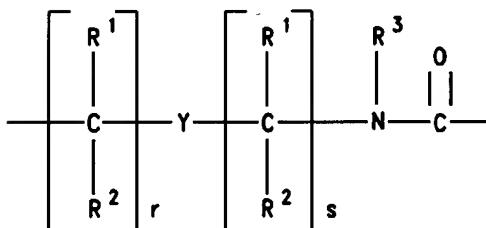
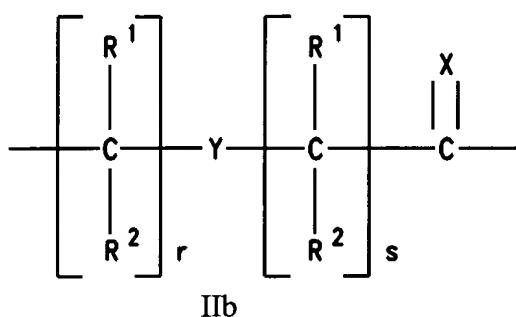
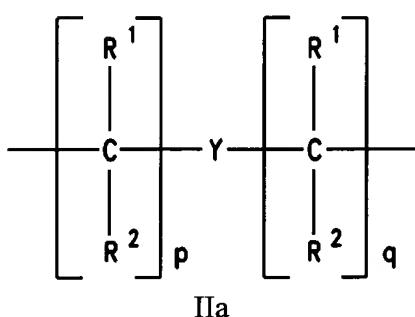
occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13} , if present, is a conjugate; and
a is 0 or 1;

A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+ ; or

(b) A is a group of formula (IId) and B is CH;



where:

X is O, S, Se, NR^3 , CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4 ;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, (C_1-C_4) alkyl, hydroxy-substituted (C_1-C_4) alkyl, alkoxy-substituted (C_1-C_4) alkyl,

alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_y$;

D is $(CR^6R^7)_z$; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR³R⁴ and SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

R³ and R⁴ independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino; and

R⁵ is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C_1-C_6) alkyl; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

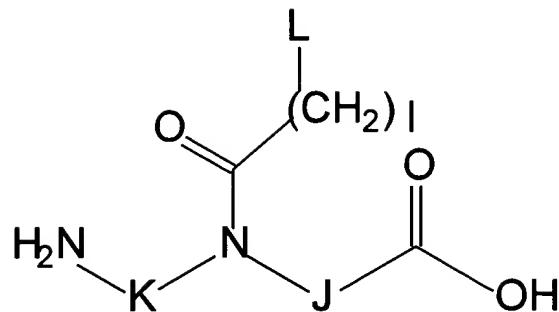
F independently is NHR³ or NPgR³, where Pg is an amino protecting group; or

F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

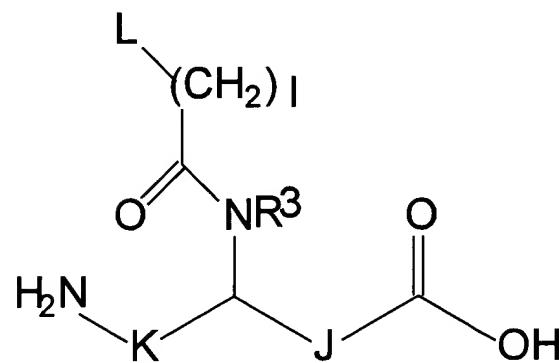
at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator,

or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a linking moiety; and wherein at least one of said groups C or said groups D include a conjugate.

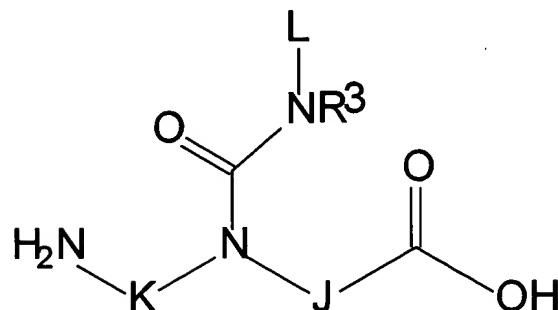
47. (Amended) A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:



or formula:



or formula:



wherein:

L is $\text{R}^{12}(\text{R}^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, ($\text{C}_1\text{-C}_4$) alkanoyl, a naturally occurring nucleobase, a non-naturally

occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R¹³, if present, is a conjugate; and
a is 0 or 1;

K is (CR⁶R⁷)_z;

J is (CR⁶R⁷)_y; wherein:

R⁶ and R⁷ are independently hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴ and SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio or amino;

R⁵ is hydrogen, a conjugate, (C₁-C₆) alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆) alkyl; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

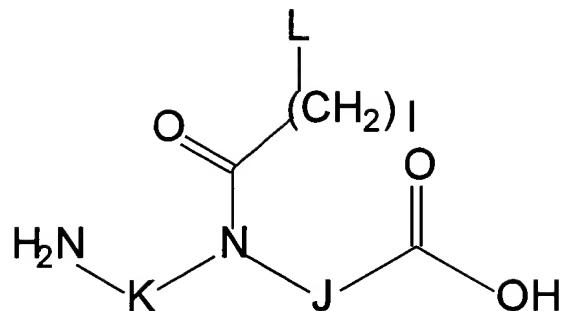
l is an integer from 1 to 5; and

at least one of L and R₃ comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

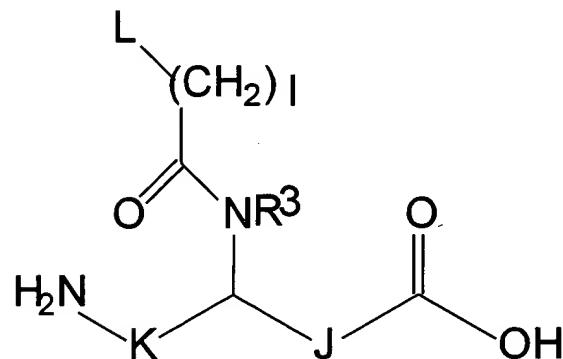
wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R³, R⁴, R⁵, R⁶, and R⁷ is a conjugate.

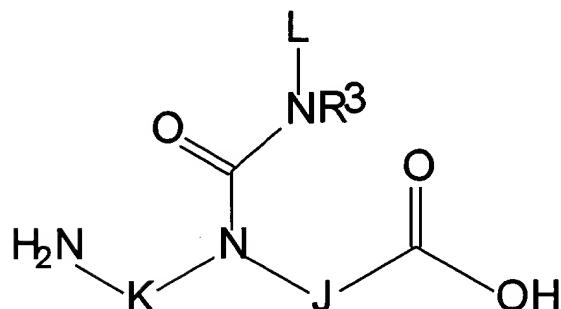
48. (Amended) A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:



or formula:



or formula:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13} , if present, is a conjugate; and
a is 0 or 1;

K is $(CR^6R^7)_z$;

J is $(CR^6R^7)_y$; wherein:

R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino;

R^5 is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C_1-C_6) alkyl; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

l is an integer from 1 to 5; and

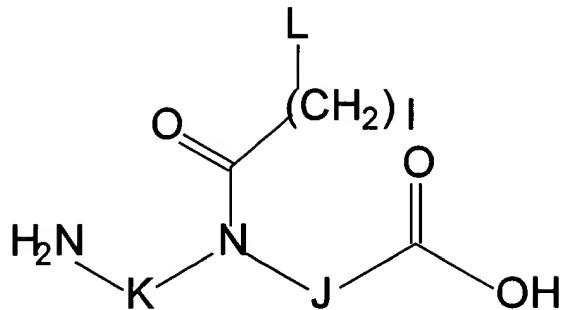
at least one of L and R3 comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric

compound selected from polymeric amines, polymeric glycols and polyethers;

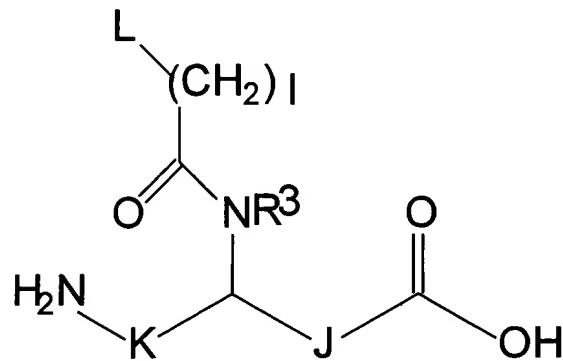
wherein said conjugate optionally includes a linking moiety; and

wherein at least one of said group K or said group J includes a conjugate.

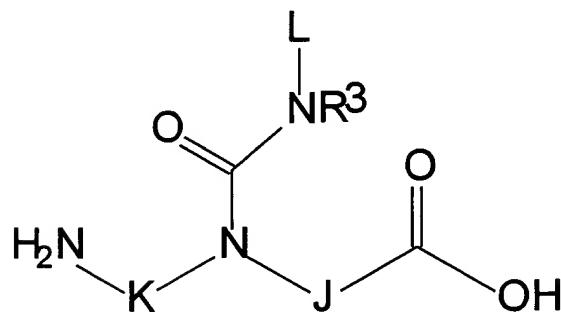
49. A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:



or formula:



or formula:



wherein:

L is $\text{R}^{12}(\text{R}^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a non-naturally

occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R¹³, if present, is a conjugate; and
a is 0 or 1;

K is (CR⁶R⁷)_z;

J is (CR⁶R⁷)_y; wherein:

R⁶ and R⁷ are independently hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴ and SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio or amino;

R⁵ is hydrogen, a conjugate, (C₁-C₆) alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆) alkyl;
each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

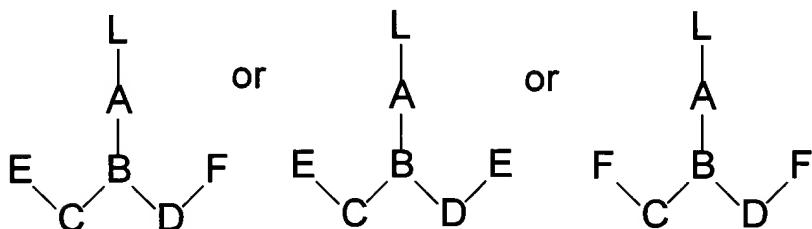
l is an integer from 1 to 5; and

at least one of L and R3 comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein said group R³ is a conjugate.

50. (Amended) A compound having one of the following formulas:



wherein:

L is R¹²(R¹³)_a; wherein:

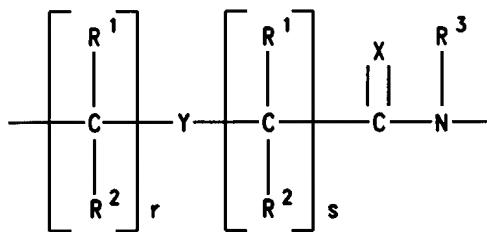
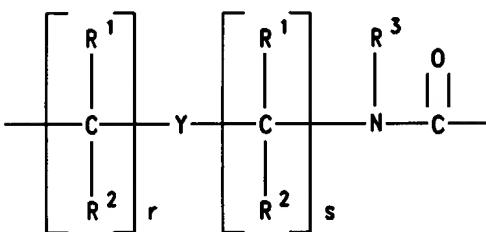
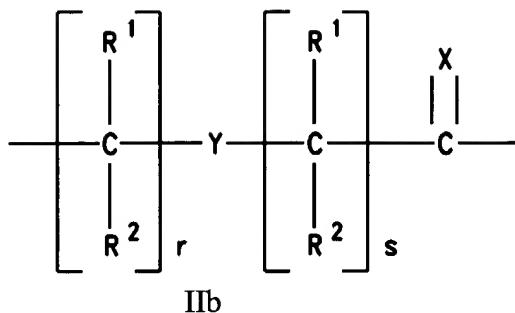
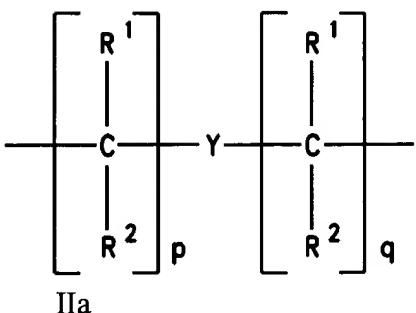
R¹² is hydrogen, hydroxy, (C₁-C₄) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R¹³, if present, is a conjugate; and

a is 0 or 1;

A and B are selected such that:

- (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R³N⁺; or
- (b) A is a group of formula (IId) and B is CH;



IIc

IId

where:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R¹ and R² independently are hydrogen, (C₁-C₄) alkyl, hydroxy-substituted (C₁-C₄) alkyl, alkoxy-substituted (C₁-C₄) alkyl, alkylthio-substituted (C₁-C₄) alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is (CR⁶R⁷)_y;

D is (CR⁶R⁷)_z; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴ and

SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system; R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio or amino; and R⁵ is hydrogen, a conjugate, (C₁-C₆)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆)alkyl; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

F independently is NHR³ or NPgR³, where Pg is an amino protecting group;

or

F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a linking moiety.

~~New claims 51 and 52 have been added:~~

51. (New) A peptide nucleic acid conjugate of claim 37 wherein one of Q or I comprises a conjugate, wherein said conjugate is polylysine.

52. (New) A peptide nucleic acid conjugate of claim 37 wherein one of A, A_m, L or L_m comprises a conjugate, wherein said conjugate is polylysine.